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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/716,356

11/21/2000

Shimpei Ushio

USHIO-2

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09/21/2005

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/716,356

Applicant(s)

USHIO ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4-9 and 18-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,2,4-9 and 19 is/are allowed.
- 6) ☒ Claim(s) 18 and 20-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Status of the Claims***

1. Currently, claims 1, 2, 4-9, and 18-52 are pending and under consideration in this application. In the prior action, claims 1, 2, and 4-9, and 19 were indicated to be allowable, and claims 18 and 20-52 were rejected. The Applicant present arguments in traversal of the rejections in the Response filed on August 19, 2005.

### ***Claim Objections***

2. **(New Objection)** Claims 22-52 are objected to because of the following informalities: these claims read on composition of claim 18, wherein “said biologically active compound” is further identified. Claim 18 has been amended to read on composition comprising a biologically active IL-18, and an optional “second biologically active compound.” While it appears that the biologically active compounds of the indicated claims are the “second biologically active compounds” of claim 18, such is not stated in the claims. For clarity, the dependent claims should use the same language as used in the claim from which they depend, and refer to the compounds in these claims as “said second biologically active compound.”

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. **(Prior Rejection- Maintained)** Claims 18, 20, and 21-52 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising SEQ ID NO: 6, or for derivatives thereof varying from SEQ ID NO: 6 by one amino acid residue, does not reasonably provide enablement for a composition comprising any homologue of the sequence that maintains the biological activities and other characteristics required by claim 18. The Applicant traverses the rejection of claims 18 and 20-52 under 35 U.S.C. 112 first paragraph for exceeding the scope of enablement on by asserting that the identification of homologues according to the claimed invention would involve no more than routine experimentation.

In support of their arguments, the Applicant has submitted a declaration by a Dr. Akira relating to the IL-18 in a European application, a copy of which has not been presented or made of record. During the course of the discussion in the Declaration reference is made to sequences and examples not present in the present application. It is therefore not clear what information the declaration is based upon. However, it is noted that the Declaration, as well as the referenced teachings of Watson et al. (Response, page 4), asserts that it would have been routine in the art to make and screen for homologues to the disclosed protein. While it may have been routine for those in the art to make mutants of SEQ ID NO: 6, and to screen such for functional homologues of the protein, such does not demonstrate that the Applicant has enabled those in the art to make and use homologues of SEQ ID NO: 6 having each of the functional requirements set forth in the claims without experimentation.

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As was indicated in the prior actions, there is little guidance presented in the application as to what modifications may be made to the proteins to maintain their activity, there is no disclosure of any homologue falling within the scope of the claims, or any identification of any sequence or structure that correlates with any of the provided functions or functional characteristics. Further, the art teaches the unpredictability in the modification of proteins. These teachings are supported by the later teachings of the WO 03/057821 (a post-filing reference cited by the Applicant on page 6 of the Response). This reference provides some guidance in what residues of the protein may be modified, and what the effects of such modification may have. See e.g., pages 78-86. However, even upon the identification of several residues that may be involved in receptor binding, the reference makes no assertions as to the effects that modifications to the identified residues would have on the protein's function. See e.g., page 85 (stating that changes to amino acids involved in receptor contact "would result in alteration of IL-18 activity by either increasing or decreasing binding," and indicates that the use of the homologue would depend on the effects resulting from the modification without identifying what these effects would be in a case to case basis). The reference therefore supports the teachings of unpredictability.

The Applicant also asserts that the teachings of Taniguchi illustrate that a homologue falling within the scope of the claims does exist. However, it is noted that this reference teaches a murine IL-18, which the Applicant has previously argued does not fall within the scope of the claims. See, Response of November 2003, pages 16-17. Thus, while the reference does teach a homologue of the claimed IL-18, the reference teaches a homologous protein not falling within the scope of the claims. Further, while the homologue of the reference does have the

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ability to induce IFN- $\gamma$  production, it is not clear that the proteion meets the additional functional limitations set forth in the claim, or that the 100-fold reduced capability to induce such produciton meets the requirement of the claims that the homologue has "substantially the same physiochemical properties and biological activity" as SEQ ID NO: 6. Nor do the teachings of the reference provide much information in the way of what residues are required for the protein's function. Thus, while the reference does teach a homologue of SEQ ID NO: 6, the homologue is not within the scope of the claims, and does not provide adequate teachings to enable those in the art to make and use any homologue to SEQ ID NO: 6 that meets each of the requirments set forth in the claims.

In view of the large scope of the claims, the limited guidance in the application, and the unpredicatability in the art, the Applicant's assertions that the devleopment of homologues according to the claimed inventions would involve only routine experimentation is not found persuasive. In order to practice the claimed invention to the full extent, those in the art would be required to determine for themselves what modifications may and may not be made to maintain protein activity. Those in the art have been provided very little guidnace by the present application in making such determiniations. Thus, for the reasons above, and the reasons of record, the Applicant's arguments are not found persuasive.

5. **(Prior Rejection- Maintained)** Claims 18, 20, and 21-52 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

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invention. As indicated in the prior actions, the Applicant has neither provided a sufficient number of species to demonstrate possession of a genus comprising any homologue of SEQ ID NO: 6 that meets each of the identified functional limitations, nor provided any identification of the members of this genus by a specific structure that correlates with the identified functions. While the Applicant has asserted that the art does disclose such homologues, neither of the two references cited is found persuasive in the instant case.

With respect to the Taniguchi reference, it is noted that this reference neither discloses a protein falling within the scope of the present claims, nor provides any further identification of those structures required for the activity of SEQ ID NO: 6 than are provided in the present application. While the teachings of WO 03057821 do provide additional teachings relating to the relationship between certain structures and the function of IL-18, the reference is not relevant to the teachings of what was known at the time of the present application as the reference was not published until three years after the present application. Further, even if the teachings of the reference were known at the time of filing, the reference does not identify any specific homologue of SEQ ID NO: 6, or provide more than a suggestion as to what residues may be modified with the hope of achieving a particular functional result.

Because the present application provides only a single example of a protein falling within the scope of the present claims, and because there is no identification of any structure that correlates to the required functions, the rejection is maintained.

### ***Conclusion***

6. Claims 1, 2, and 4-9, and 19 are allowable over the art.

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7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

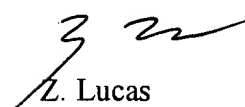
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.




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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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9/19/05